effects. Active compounds suppressed neutrophilic inflammation to levels below those seen with our positive control, a potent inducer of neutrophil apoptosis, pyocyanin. For example, in control fish, the number of neutrophils present at the site of injury at 24 h postinjury was 30.24±1.47. In pyocyanin-treated fish it was 19.04±1.93, and for one compound it was 12.33±1.85 (mean±SEM, $p<0.05$ for both treatments vs control, one-way analysis of variance (ANOVA) with Bonferroni post-test correction, n = 49, 24 and 9, respectively). These compounds are under further investigation for their ability to modulate human neutrophil function and will be assessed for enhancement of resolution of inflammation in mammalian models of neutrophilic pulmonary inflammation.

Conclusions These data show the ability of this model to identify novel therapeutics with dramatic immunomodulatory properties. Some of these compounds may be useful lead compounds for the identification of novel therapeutic entities.

S81 A COMPARISON OF TWO METHODS TO QUANTIFY TENASCIN C EXPRESSION WITHIN THE RETICULAR BASEMENT MEMBRANE OF PAEDIATRIC ENDOBRONCHIAL BIOPSIES

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Introduction Tenascin C (TN) is an extracellular matrix glycoprotein with increased expression in the epithelial reticular basement membrane (RBM) in adult asthma. The RBM is thicker in preschool children who wheeze, when compared with age-matched non-wheezing controls.[1] We believe that increased TN expression may be a more sensitive marker for severe preschool wheeze (and future asthma) than RBM thickness alone.

Aim To use two methods of quantifying immunohistochemically detected TN expression within the RBM in endobronchial biopsies (EBs) stained with immunoperoxidase.

Methods EBs from preschool children undergoing clinically indicated bronchoscopy were obtained from both wheezers (n = 29, median age 22.5 months) and non-wheezers (n = 10, median age 25 months). Wheezers were divided into confirmed wheeze (CW, n = 15) or reported wheeze (RW, n = 14) based on parent identification using a video questionnaire. Paraffin sections of 5 μm were cut and stained for TN as previously described.[2] For TN quantification, method 1 calculated the mean of all TN thickness measurements at 20 μm intervals along the whole RBM, using computer-aided image analysis.[3] Method 2 used a semi-quantitative scale to grade the TN-positive proportion of RBM: grade 1 (<1/3), grade 2 (1/3–2/3) and grade 3 (≥2/3).[4] All biopsies were assessed by a single, blinded observer. Non-parametric tests were used to analyse the data.

Results Method 1 showed a significant difference in TN thickness between CW and controls ($p = 0.01$), but method 2 showed no group differences ($p = 0.45$). Intraobserver repeatability (coefficient of variation) for method 1 was 0–34%; the intraclass correlation coefficient for repeated measurements for method 2 was 0.93 ($p<0.0001$). There was no correlation between age and TN expression in the controls.

Conclusion There was increased TN in the RBM of preschool CW compared with controls using method 1. However, in contrast to direct measurements of RBM thickness, there is large variability in TN expression within the RBM which impacted on reliability of both the above methods; method 1 had poor repeatability and method 2 had poor discriminative power. Stereological techniques are being evaluated to overcome these limitations.

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New observations from physiology

S82 CLINICAL USEFULNESS OF MEASURING NEURAL RESPIRATORY DRIVE FOR IDENTIFICATION OF DETERIORATION IN ACUTE EXACERBATIONS OF COPD

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Introduction Early discharge schemes and transfer of acute care into the community setting are strategic objectives for the National Health Service (NHS), with acute exacerbations of chronic obstructive pulmonary disease (AECOPD) identified as a key area. The ability to predict accurately response to treatment and early detection of clinical deterioration are therefore essential. We hypothesised that neural respiratory drive (NRD), as represented by parasternal muscle electromyography (EMG_{para}), could be used as a novel clinical tool to identify clinical change in AECOPD.

Method Emergency admissions to the acute medicine ward with AECOPD were enrolled within 24 h of admission. Repeated measures of EMG_{para} were performed during their hospital admission and correlated with clinical course as assessed by the supervising clinician, blinded to the EMG_{para} data. EMG_{para} was normalised to $EMG_{para\%max}$ obtained during a maximal sniff manoeuvre performed at the time of readings, and data were analysed off-line as peak root mean squared per breath[1] to produce an $EMG_{para\%max}$.

Results 25 patients (27% male), mean age 74 (8.5) years and forced expiratory volume in 1 s (FEV_1) 0.57 (0.29) litres had baseline data recorded. All patients were able to tolerate EMG_{para} testing on study days, in contrast to 30% of patient unable or unwilling to complete FEV_1 testing. Repeat readings on consecutive days led to 30 pairs of data. On five occasions patients were deemed to have clinically deteriorated and on 25 occasions deemed to have improved. Changes in heart rate (HR), oxygen saturations (SpO_2), respiratory rate (RR), FEV_1, Medical Early Warning Score (MEWS) and NRD are shown in table 1.

Abstract S82 Table 1 Differences (mean±SD) in physiological variables between "improvers" and "deteriorators"

	ΔHR	ΔSpO_2	ΔRR	ΔFEV_1	ΔMEWS	ΔEMG_{para}	Δ$EMG_{para\%max}$
"Deteriorators"	1.4±7.4	1.8±2.0	4.80±6.69	0.1±0.1	0.60±0.55	6.67±17.13	5.34±4.24
"Improvers"	−2.56±10.9	0.48±2.5	−1.40±3.86	0.06±0.1	−0.36±0.81	−1.88±5.72	−2.65±8.20
Mean difference	3.96	1.32	6.20	0.06	0.96	8.57	7.98
p Value	0.35	0.25	0.11	0.5	0.011	<0.01	<0.01

EMG_{para}, parasternal muscle electromyography; FEV_1, forced expiratory volume in 1 s; HR, heart rate; MEWS, Medical Early Warning Score; RR, respiratory rate; SpO_2, oxygen saturations.

Conclusion These data show the feasibility of measuring NRD in the acute care setting. There were no significant differences observed between "improvers" and "deteriorators" in the standard physiological measurements performed in the acute care setting. Although there was a significant difference in MEWS, the mean increase in the patients who deteriorated was <1 and thus insufficient to prompt a clinical response. However, both EMG_{para} and NRD showed discrimination between "mprovers" and "deteriorators". Further work is currently ongoing to investigate the usefulness of NRD for identifying treatment failure and early deterioration in AECOPD.

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S83 FACEMASK SPIROMETRY IN PATIENTS WITH BULBAR MOTOR NEURON DISEASE

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Background Forced vital capacity (FVC) has predictive value for prognosis in motor neuron disease (MND) and is used as a decision aid when starting non-invasive ventilation (NIV). However, bulbar involvement makes it impossible for many people with MND to perform the manoeuvre due to mouth leaks or difficulty inserting and gripping a mouthpiece.

Aim To investigate the use of a facemask to measure FVC and compare it with spirometry using a conventional mouthpiece, in people with MND and bulbar symptoms.

Methods People with MND and bulbar symptoms (dysphagia, dysarthria or drooling with signs of increased jaw jerk, fasciculation or spasticity of tongue) attending a follow-up clinic had facemask spirometry if there was a suspicion that the results of mouthpiece measurement were suboptimal. The best of three attempts were recorded for each technique in the seated position.

Results In a 9-month period, 27 people (13 men), with a mean age of 64 (SD 13.6) years, had both methods of measuring spirometry attempted. Eleven of the 27 were using NIV. All managed with a facemask; 14 failed to record anything on the mouthpiece. Facemask FVC was 1.84 litres (SD 0.77, n = 27). Facemask FVC in those who failed with the mouthpiece was 1.63 litres (SD 0.70, n = 14). In those who were able to record FVC with the mouthpiece FVC was 1.42 litres (SD 0.65, n = 13). When FVC was recorded with both methods, FVC was greater using the facemask in all but one person (see fig 1). The mean difference was 0.65 litre (SD 0.43) $p<0.001$.

Conclusion In these patients facemask spirometry was acceptable to patients and none failed to record results, while 52% could not produce any result with a mouthpiece. The mean difference between the measures when both were available was clinically significant and could affect decision making regarding NIV. A formal study is required to confirm these findings, extend them to patients without obvious bulbar symptoms and exclude order effects.

S84 QUADRICEPS ENDURANCE IS REDUCED IN FIBROTIC IDIOPATHIC INTERSTITIAL PNEUMONIA

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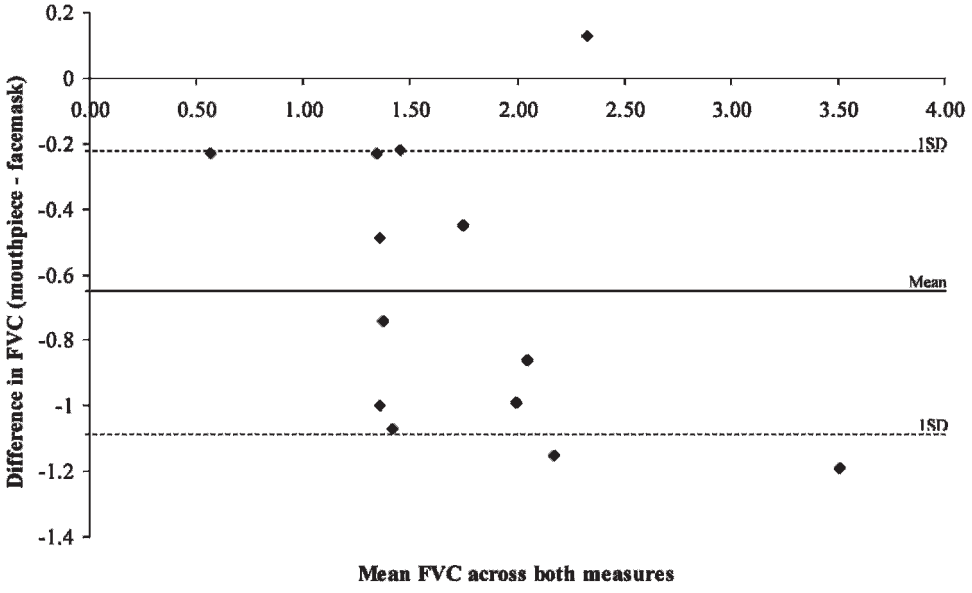
Background Fibrotic idiopathic interstitial pneumonia is characterised by exertional dyspnoea and reduced exercise capacity, both attributed to pulmonary function deterioration. Little is known about the role of reduced peripheral skeletal muscle function as a factor in exercise capacity in this condition.

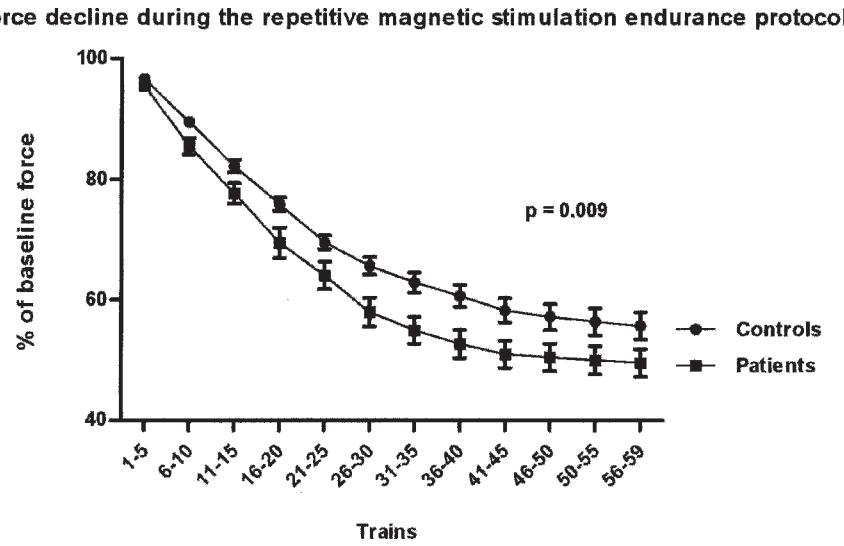
Aims To determine the presence of reduced quadriceps strength and/or endurance and its relationship to exercise capacity in patients with fibrotic idiopathic interstitial pneumonia.

Methods We studied 25 patients with fibrotic idiopathic interstitial pneumonia, forced vital capacity (FVC) mean (SD) 78.7 (14.0) % predicted, TL_{CO} mean (SD) 40.3 (10.9) % predicted, and 25 age-matched healthy controls. We measured fat-free mass, respiratory muscle strength, voluntary quadriceps strength (QMVC), twitch quadriceps force (TwQ) and quadriceps endurance with a protocol consisting of repetitive magnetic stimulation of the quadriceps using a special coil with 60 trains (2 s on, 3 s off) over 5 min. The 6 minute walking test (6MWT) was measured as an indicator of exercise capacity.

Results Both groups had comparable fat-free mass. There were no significant differences between patients and controls in respiratory muscle function (sniff nasal inspiratory pressure (SNIP), maximum



Abstract S83 Figure 1 Bland–Altman plot of forced vital capacity (FVC) using both the mouthpiece and facemask (n = 13).



Abstract S84 Figure 1.

inspiratory pressure (MIP) and maximum expiratory pressure (MEP)) and quadriceps strength measurements (QMVC mean (SD) 75.3 (18.3) vs 78.1 (16.5) % predicted and TwQ 8.0 (2.4) kg vs 9.8 (3.3) kg, patients vs controls). However, the force decline of the quadriceps during the endurance protocol was significantly greater in patients (fig 1). There was a significant difference in the 6MWD (489 (88.8) m vs 616 (74.6) m, patients vs controls, $p<0.0001$). The time to fall to 70% of baseline force ($T_{70\%}$) in the endurance protocol correlated significantly with the 6MWD in controls ($r^2 = 0.35$ $p = 0.016$) but not in patients. In a stepwise multiple regression analysis, basal PaO_2 was the only significant predictor of the 6MWD in patients ($r^2 = 0.2$ $p = 0.022$).

Conclusion Fibrotic idiopathic interstitial pneumonia significantly affects quadriceps endurance.

S85 COMPARISON OF EAR AND FINGER OXIMETRY READINGS DURING AMBULATORY OXYGEN ASSESSMENTS

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Ambulatory oxygen requirements are routinely assessed and titrated using portable finger pulse oximetry (BTS 2006). In practice, we found that movement artefact or reduced circulation may adversely affect the measurement. Whilst using ear oximetry alongside finger oximetry on patients it was noted that the ear readings were often higher. These differences could potentially affect the prescription of ambulatory oxygen.

Objective To evaluate the use of portable oximetry measurements taken from the ear and finger during ambulatory assessments.

Method Over a period of 18 months 265 non-smoking patients referred for ambulatory oxygen assessment had ear and finger pulse oximetry measurements recorded before, during and after a 6 minute walking test using the Konica Minolta Pulsox. The finger oximeter was sited on the middle finger of the right hand; the ear probe on the right ear lobe after vasodilation with thurfyl nicotinate (Transvasin) cream. Patients were instructed to walk at a comfortable pace for up to 6 min. Pretest and post-test saturation and pulse were simultaneously recorded from the finger and ear oximeters.

Results There was a significant difference between ear and finger measurements both before and after exercise ($p<0.001$ for both). The mean difference before exercise was 1.9% (95% CI −1.75% to 5.5%), and postexercise was 2.8% (95% CI −3.5% to 9.1%). Earlobe measurements tended to be higher than finger measurements. There were no significant differences noted in pulse rate measurements. The observed differences in oxygen saturation could have altered the clinical outcome in 25% of the patients assessed (66 of 265).

Conclusion There are clinically and statistically significant differences in the ear and finger probe measurements. In our observational study, an extra 25% of patients met the criteria for ambulatory oxygen therapy using finger oximetry compared with earlobe readings. This may impact not only on the patient, but also on the national ambulatory oxygen budget.

S86 THE EFFECT OF ACUTE HYPOXIA ON QT INTERVAL IN RESPIRATORY PATIENTS UNDERGOING FITNESS TO FLY TESTS

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Background Previous studies have shown that acute exposure of healthy subjects to hypoxic conditions prolongs cardiac repolarisation (QT interval or QTc when corrected for heart rate) and that the magnitude of desaturation correlates with lengthening of the QTc interval. We aimed to assess whether this occurred in patients with chronic respiratory disease who were exposed acutely to hypoxic conditions.

Methods Patients with chronic respiratory disease undergoing ''fitness to fly'' tests, at a single centre, between April 2008 and February 2009, were retrospectively identified. Tests were performed by exposing patients to 15% O_2 for 20 min with assessment of blood gases and 12-lead ECG prior to and at the end of the hypoxic exposure period.

Results 101 patients were included (58 females and 43 males; median age 57 years). 40 (39.6%) patients had a diagnosis of interstitial lung disease, 12 (11.9%) bronchiectasis, 12 (11.9%) chronic obstructive pulmonary disease (COPD), 8 (7.9%) sarcoidosis, 7 (6.9%) cystic fibrosis, 6 (5.9%) systemic sclerosis, 5 (5.0%) asthma, 3 (3.0%) extrinsic allergic alveolitis and 8 (7.9%) suffered

from other conditions. 15 (14.9%) also had pre-existing cardiac disease. Mean PaO_2/SaO_2 fell from 10.56 kPa/95.8% on air to 6.82 kPa/87.2% on 15%O_2 ($p<0.001$). ECG analysis revealed that the hypoxic challenge resulted in a significant increase in heart rate (from 83.2 to 86.9 bpm; $p<0.001$), a significant decrease in QT interval (from 357.8 to 348.8 ms; $p<0.001$) and a significant decrease in PR interval (from 161.2 to 158.0 ms; $p = 0.01$). However, there was no significant change in QTc (from 415.2 to 417.0 ms; $p = 0.50$). A significant correlation was noted between decrease in QT interval and decrease in PaO_2 ($p = 0.01$); however, there was no correlation between change in QTc and change in either PaO_2 or SaO_2. There was no difference in response between those with and without pre-existing cardiac disease.

Conclusion This cohort of 101 patients with chronic respiratory disease demonstrated a decrease in QT interval consistent with an increased heart rate in response to hypoxic challenge. This is different from the response in healthy subjects and may represent an effect of hypoxic preconditioning. Fitness to fly tests do not appear, on the basis of ECG evidence, to be hazardous for patients.

S87 SHALLOW BREATHING AND CYST-LIKE SPACES AUGMENT DEADSPACE VENTILATION IN COALWORKERS' PNEUMOCONIOSIS

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Background Coalworkers' pneumoconoisis (CWP) traditionally presents with breathlessness secondary to increased exercise ventilation. We examined the mechanisms and estimated their likely magnitudes in men referred for assessment by the local Pneumoconiosis Medical Panel.

Subjects, Methods and Underlying lung function Lung function and the ventilatory responses to progressive submaximal treadmill exercise were assessed in 54 ex-coalminers with radiographic pneumoconiosis and exertional dyspnoea, 9 men with presumed centrilobular emphysema (PCE) and 44 men with normal lung function, despite working in dusty occupations. The latter formed a comparison group (CG). Exercise ventilation was at an O_2 uptake of 1.0 l/min (45 mmol/min, designated $V'ex_{st}$). The breathing pattern was in terms of ventilation and respiratory frequency at a V′ex of 30 l/min (Vt_{30} and fR_{30}, respectively). Ventilation was interpreted using a model with terms for alveolar ventilation, and airway and alveolar deadspace ventilation (V′aw.ds and V′alv.ds, respectively).[1]

Results The lung function of the men with CWP exhibited moderate airways obstruction and defective gas transfer, similar to that reported for coalworkers with irregular opacities.[2] It differed significantly from that for the men with PCE. On exercise, the $V'ex_{st}$ in CWP and in PCE was increased compared with CG (means 34.6, 33.6 and 23.4 l/min, respectively, $p<0.05$). In CWP the Vt_{30} was reduced. From the model, in men with CWP 17% of the increase in exercise ventilation reflected additional alveolar ventilatory drive (possibly from the low transfer factor), 24% a shallow breathing pattern and 59% a significant V′alv.ds, possibly ventilation of cyst-like spaces (not PCE).

Conclusions Up to 41% of the increase in ventilation could be amenable to therapy. To this end, the functional assessment should include breathing pattern during treadmill exercise. The neuropharmacology of control of breathing pattern should be explored. The findings have implications for other chronic lung disorders.

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In vivo and in vitro modelling in acute lung injury

S88 SOURCES OF INCREASED PLASMA SOLUBLE TNF RECEPTORS DURING INJURIOUS MECHANICAL VENTILATION IN MICE

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Introduction Increased plasma levels of soluble tumour necrosis factor (TNF) receptors (sTNFRs) are associated with mortality in patients with acute respiratory distress syndrome (ARDS) ventilated with high tidal volumes (V_Ts). These increases are considered to reflect either systemic inflammation, or decompartmentalisation of elevated intra-alveolar sTNFRs into the circulation due to alveolar–capillary barrier dysfunction. However, the contribution of mechanical ventilation per se has not been well defined. We have previously shown in an in vivo mouse model of pure ventilator-induced lung injury that sTNFRs can leak into the alveolar space from the plasma.[1] Consequently, it is unclear where increases in plasma sTNFRs would originate.

Methods Anaesthetised C57BL6 mice were ventilated with high (36–41 ml/kg) or low V_T (8–9 ml/kg) for up to 2 h. Upon termination, plasma samples were taken for quantification of sTNFR p55 and p75 (ELISA), and lungs were harvested for flow cytometric analysis of lung cell suspensions for TNFR p55 and p75 expression.

Results Plasma sTNFR p55 levels substantially increased at 1 h with high V_T compared with low V_T (see table 1), but declined at 2 h. A similar trend, though not statistically significant, was observed for sTNFR p75. After 2 h of high V_T ventilation, pulmonary endothelial cells and lung-marginated monocytes had decreased surface expression of TNFRs. Lung-marginated neutrophils exhibited no changes in sTNFR expression.

Conclusions These data indicate that injurious ventilation can induce systemic sTNFR changes in the absence of pre-existing lung/systemic pathology. The increases in plasma sTNFRs occur earlier than previously reported sTNFR elevation in the alveolar space,[1] and therefore cannot be explained by decompartmentalisation of elevated intra-alveolar sTNFRs. Conversely, our data strongly suggest that injurious lung stretch directly activates pulmonary intravascular cells (endothelial cells and lung-marginated monocytes), inducing shedding of cell surface TNFRs within the

Abstract S88 Table 1

	Low V_T	High V_T
Plasma (1 h)		
TNFR p55 (pg/ml)	1,120 ± 152	1,910* ± 480
TNFR p75 (pg/ml)	8,650 ± 2,330	14,900 ± 10,900
Endothelial cells (2 h)		
TNFR p55 (MFI)	22.7 ± 8.01	11.7* ± 4.46
TNFR p75 (MFI)	7.50 ± 0.920	3.16* ± 2.52
Lung-marginated monocytes (2 h)		
TNFR p55 (MFI)	48.4 ± 5.83	31.9* ± 4.53
TNFR p75 (MFI)	84.7 ± 31.0	57.0 ± 21.8
Lung-marginated neutrophils (2 h)		
TNFR p55 (MFI)	35.1 ± 6.00	36.3 ± 3.99
TNFR p75 (MFI)	7.48 ± 6.88	7.30 ± 5.85

n = 3–7.
*$p<0.05$ vs low V_T; t tests; mean ± SD.
MFI, mean fluorescence intensity with isotype control values subtracted; TNFR, tumour necrosis factor receptor; V_T, tidal volume.